DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: AUG 21 2002

From: Director, Division of Standards and Labeling Regulations, Office of Nutritional Products, Labeling and Dietary Supplements, HFS-820

Rec'd 8/30/02 jb

Subject: 75-Day Premarket Notification of New Dietary Ingredients

To: Dockets Management Branch, HFA-305

New Dietary Ingredient:	S-adenosylmethionine (SAMe)
Firm:	US Botanicals
Date of Follow-up Letter:	September 26, 2001

On September 26, 2001, the Food and Drug Administration (FDA) attempted to send the attached letter to Mr. Dave Brown, US Botanicals, Mesa, Arizona, in follow up to a 75-day premarket notification for S-adenosylmethionine (SAMe) dated October 14, 1997. This letter was returned to FDA as undeliverable due to a wrong address. The address FDA used was the only one we had which was in effect for US Botanicals in October 1997. All of our efforts to identify correct land mail and electronic mail addresses and phone or fax numbers were unsuccessful. Therefore, FDA was unable to notify US Botanicals about our concerns.

We request that this memorandum and the attached letter and photocopy of FDA's postmarked envelope used to mail Mr. Brown the letter be placed on public display in docket number 95S-0316 as soon possible. Please also cross-reference this new posting to Rpt 19 that represents Mr. Brown's October 1997 notification that is filed in the same docket number. It is hoped that Mr. Brown or another representative of US Botanicals will see this letter via this avenue. Thank you for your assistance.

Felicia B. Satchell

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Attachments

95S-0316

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DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Washington, DC

SEP 26 2001

Mr. Dave Brown
US Botanicals
1611 N. Sawyer
Mesa, Arizona 85207

Dear Mr. Brown:

This is in follow up to your letter to the Food and Drug Administration (FDA) dated October 14, 1997, making a submission of a new dietary ingredient pursuant to 21 U.S.C. 350b(a)(2) [section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)]. Your letter notified FDA of your intent to market a dietary supplement product containing the new dietary ingredient called S-adenosylmethionine (SAMe). We initially filed your notification without comment in docket number 95S-0316 with FDA Dockets Management Branch, and the information in your notification was disclosed to the public after January 20, 1998.

As stated under 21 U.S.C. 350b(a)(2), the premarket notification process requires that a manufacturer or distributor of a dietary supplement that contains a new dietary ingredient have a basis for determining that it will reasonably be expected to be safe, when used under the conditions recommended or suggested in the product's labeling. According to 21 CFR § 190.6(f), if FDA does not respond within the 75-day premarket notification period, this does not constitute a finding by the agency that the new dietary ingredient or a dietary supplement containing it is safe or not adulterated. Also, FDA is not precluded from commenting on a new dietary ingredient after it is marketed.

Since the date of your original notification, FDA has become aware of information that raises concerns about whether a dietary supplement containing SAMe will reasonably be expected to be safe if used by certain subpopulations of consumers. For example, the scientific literature[1] suggests that persons who have a bipolar major affective disorder (manic-depressive disease) may experience mood switching from depression to hypomania when supplemented with SAMe. The scientific literature also suggests that SAMe displays neuropsychiatric properties. There is the potential for serious health risks for persons already taking drugs or other products that may adversely interact with a dietary supplement containing SAMe at the recommended intake of 1200 milligrams per day cited in your

[1] Baldessarini, Ross J.: Neuropharmacology of S-Adenosyl-L—Methionine, *The American Journal of Medicine*, 83(suppl 5A):95-103, November 20, 1987.

notification. In addition, other journal articles[2,3,4] that were included in your notification stated that taking supplements of SAMe at daily levels ranging from 400 to 1200 mg may cause unwanted side effects (e.g., heartburn, nausea, and other gastrointestinal symptoms).

Under 21 U.S.C. 321(n) and 343(a) [sections 201(n) and 403(a) of the Act, respectively], an article is misbranded if its labeling fails to reveal material facts about the consequences of using the product under its labeled conditions of use. FDA has interpreted these sections to require warning label statements where an ingredient has presented special health risks to consumers under certain conditions of use. Therefore, failure to reveal on the labeling information concerning serious adverse effects attendant to the use of a dietary supplement under conditions of use (e.g., for those who have particular medical condition or are taking certain medications) when the scientific evidence indicates that there are potential health risks may render the dietary supplement misbranded under 21 U.S.C. 321(n) and 343(a) [sections 201(n) and 403(a) of the Act, respectively]. FDA encourages US Botanicals by its next label printing to include an appropriate warning label statement on all dietary supplements containing SAMe that it manufacturers or distributes now or in the future.

One of the "B" list 2001 priorities for the Center for Food Safety and Applied Nutrition, FDA is to develop guidance or regulations on safety information and material fact labeling for dietary supplements. Work is under way to accomplish this goal. However, the absence of such guidance or regulations at this time does not dismiss manufacturers and distributors from their responsibility to ensure that the dietary supplements they market are safe and properly labeled.

If you have any questions concerning this matter, please contact me at (202) 205-4168.

Sincerely yours,

Felicia B. Satchell

Felicia B. Satchell
Director
Division of Standards
and Labeling Regulations
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety
and Applied Nutrition

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[2] König, Benno: A Long-Term (Two Years) Clinical Trial with S-Adenosylmethionine for the Treatment of Osteoarthritis, *The American Journal of Medicine*, 83(suppl 5A):89-94, November 20, 1987.

[3] Caruso, Innocenzo and Pietrogrande, Vincenzo: Italian Double-Blind Multicenter Study Comparing S-Adenosylmethionine, Naproxen, and Placebo in the Treatment of Degenerative Joint Disease, *The American Journal of Medicine*, 83(suppl 5A):66-71, November 20, 1987.

[4] Berger, Rainer and Nowak, Horst: A New Medical Approach to the Treatment of Asteoarthritis: Report of an Open Phase IV Study with Ademethionine (Gumbaral), *The American Journal of Medicine*, 83(suppl 5A):84-88, November 20, 1987.

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Public Health Service
Food and Drug Administration (HFS-820)
200 C Street SW
Washington DC 20204

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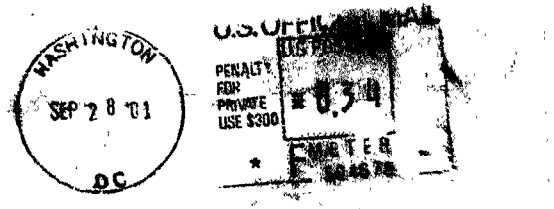

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Mr. Dave Brown
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WRONG ADDRESS

Dk 9 3000

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